REMARKS

Applicants respectfully request favorable reconsideration in view of the herewith presented amendments and remarks.

Claims 1-55 are pending in this application. Claim 47 is withdrawn from consideration. Claims 1-46 and claims 48-55 are rejected.

35 U.S.C. §112 Rejections

Claims 1-46, and 48-55 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. In particular, the Examiner asserts that claim 1 is indefinite over the recitation "capable of hybridizing." Applicants respectfully disagree with this rejection. However, in order to expedite prosecution of this application, applicants have amended the claims to read, for example, "which hybridizes" as suggested by the Examiner, thereby obviating this rejection. Reconsideration and withdrawal of this 35 U.S.C. §112, second paragraph rejection is respectfully requested.

35 U.S.C. §102 Rejections

Claims 1 and 40 stand rejected under 35 U.S.C. §102(b) as being anticipated by Nathan, et al. (USPN: 6,057,099) for teaching a method of detecting a target nucleic acid. The Examiner contends that Nathan, et al. anticipates claims 1 and 40 as describing a method for detecting a target nucleic acid comprising formation of an RNA:DNA hybrid and further meeting the limitations of the rejected claims. Applicants respectfully disagree.

As an initial matter, applicants remind the Examiner that MPEP 2131 states that to anticipate a claim, the reference must teach every claim element. In particular, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or

inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

The Examiner specifically points to col. 21, lines 34-36 of the Nathan patent as describing "detecting the bound hybrid" (Paper No. 21; page 4). Applicants respectfully point out that the indicated section does not mention detecting a bound double-stranded nucleic acid hybrid. Rather, this section merely describes transcribing and amplifying oligonucleotide transcripts and detecting a single-stranded reporter oligonucleotide. Furthermore, it is unclear from the Nathan reference how one skilled in the art would perform the detection step.

Applicants respectfully direct the Examiner's attention to Figure 1 of the Nathan patent which describes the method of detecting the presence of a transcription reaction product that has been amplified. Although Nathan describes the ligation step as optional, it is required if the first and second oligonucleotides are complementary to only a part of the entire length of the assayed nucleic acid sequence, since transcription would not occur due to the gap. The transcription reaction product or triggering oligonucleotide is labeled as **110**, and is further amplified to obtain large quantities of the transcript or signaling oligonucleotide labeled **116**.

Briefly, the Nathan patent uses transcription and amplification steps for detecting the resulting transcription reaction product, which indirectly indicates the presence or absence of the assayed nucleic acid. The oligonucleotides act as primers which hybridize to the assayed nucleic acid. Upon the addition of reagents, transcription occurs, thereby generating a single-stranded transcription reaction product. Amplification allows the production of large quantities of transcript which is detected.

The Examiner points to claim 13, step (g) of Nathan as teaching hybrid detection but this section simply relates to the detection of a single-stranded reporter oligonucleotide sequence. "Reporter oligonucleotide" is defined at col. 3, lns. 38-44 of the Nathan patent as "an RNA oligonucleotide or an hybrid RNA/DNA oligonucleotide (an RNA oligonucleotide with some dNTPs). The reporter oligonucleotide is being produced in the amplification ensemble (see below). The production of the reporter oligonucleotide serves to indicate the presence of the assayed nucleic acid sequence in the sample." Nathan's reporter oligonucleotide is a single-stranded molecule produced as a result of transcription and amplification and is not a double-stranded hybrid comprising an RNA sequence strand hybridized to a DNA sequence strand. "Hybrid RNA/DNA oligonucleotide" according to Nathan, refers to what is more commonly known as a chimera/chimeraplast, which is a synthetic single-stranded molecule composed of RNA and DNA parts. This single-stranded transcription reaction product is exemplified in Figures 10-12 and labeled **1010**, **1110**, and **1210**, respectively.

In contrast, the method of the instant invention detects a target nucleic acid by detecting a double-stranded hybrid comprising a signal sequence probe and target nucleic acid. The capture sequence probe of the instant invention is used to capture the target nucleic acid to a solid support. Claim 1, step (d) relates to detecting the double-stranded bound hybrid and claim 40, step (b) relates to detecting a hybrid complex containing a signal sequence probe: target nucleic acid. Applicants respectfully direct the Examiner's attention to Figure 1 of the instant invention which demonstrates how the target nucleic acid is detected. In particular, antibodies that are specific for RNA:DNA hybrids are used to detect the target double-stranded nucleic acid:signal sequence probe hybrid.

Thus, the method of detection described in the Nathan patent does not detect probe:target double-stranded nucleic acid hybrid as claimed in the instant application. The method in the Nathan patent does not resemble that of the claimed invention, nor does Nathan anticipate claims 1 and 40. Applicants respectfully request that the 35 U.S.C. §102 rejection to claims 1 and 40 be reconsidered and withdrawn.

35 U.S.C. §103 Rejections

Claims 2-39, 41-46, and 48-55 have been rejected under 35 USC §103(a) as being unpatentable over Nathan, et al. (USPN 6,057,099) and in view of Shah, et al. (USPN 5,629,156). The Examiner contends that Nathan teaches the claimed method except for immobilization of the probes and detecting the probe:target hybrid by using an antibody. The Examiner further contends that the Shah patent teaches immobilization of capture probe onto a solid support. Applicants respectfully disagree with the Examiner's contentions.

As discussed above, Nathan does not anticipate or make obvious the claimed invention. The Nathan method is essentially transcription and amplification reactions and does not describe detecting double-stranded hybrids or hybrid complexes in order to determine the presence or absence of an assayed nucleic acid. Nathan describes several additional steps, *i.e.*, transcription and amplification, that are not necessary in the instant invention for one skilled in the art to detect target nucleic acids. In fact, according to MPEP 2144.04, omission of an element while retaining the essential function is not obvious. *In re Edge*, 359 F.2d 896, 149 USPQ 556 (CCPA 1966).

The Examiner has combined the Nathan reference with the Shah reference, the latter of which describes a method for determining the presence of a target nucleic acid by using

a capture-release process. The Examiner readily admits that the primary reference (i.e. Nathan, et al.) does not teach or suggest immobilization of the probes and detection of the probe:target hybrid using hybrid-specific antibodies. The Examiner attempts to reach the instant invention by combining the Shah reference with the Nathan reference to allege the claims directed to methods of detecting hybrids (i.e., claims 2-39, 41-46, and 48-55) is obvious. However, the Nathan reference does not teach or suggest the claimed invention even with the Shah reference. The deficiencies of Nathan are not overcome with Shah.

The Shah reference essentially describes a method using capture oligonucleotides and differentially releasing the target nucleic acid in order to achieve specificity. However, the combination of Nathan and Shah fails to make the present invention obvious. Nathan fails to teach or suggest an assay using (1) a signal sequence probe and capture sequence probe, where the capture sequence probe immobilizes the target nucleic acid to a solid support or (2) antibodies specific for probe:target nucleic acid hybrids for detection. In fact, it is unclear as to how the detection step is performed from reading the Nathan reference. Shah does not remedy these deficiencies. Shah also does not teach or suggest blocker probes because the analogous probe (i.e., the second capture probe) has no affinity for the first capture probes, which is a required function of the blocker probes of the present invention. Therefore, neither of the references, alone or when viewed in combination, teach or suggest the claimed method as a whole. In reading the cited references, the skilled artisan would not be able to generate the claimed method, which detects double-stranded probe:target nucleic acid hybrids. Thus, applicants respectfully request reconsideration and withdrawal of the §103(a) rejection.

CONCLUSION

Based on the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

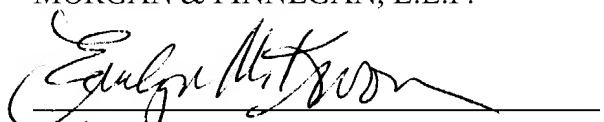
AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. 13-4500, Order No. 2629-4017. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 13-4500, Order No. 2629-4017. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

Respectfully submitted,

MORGAN & FINNEGAN, L.L.P.

Dated: February 10, 2004 By: 

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